MINUTES OF THE CANCER GUIDELINES SUBCOMMITTEE OF THE SAB EXECUTIVE COMMITTEE JANUARY 20-21, 1999

PURPOSE: The purpose of the meeting was to conduct an advisory on the draft revisions to the EPA's Proposed Guidelines for Carcinogen Risk Assessment. The meeting was held on January 20-21, 1999. The meeting was announced in the *Federal Register* for January 4, 1999 (Volume 64, Number 1, pages 167-168) (Attachment A). The background material which was distributed to the Members and Consultants prior to the meeting is incorporated as Attachments B1 through B11. The list describing the contents of Attachments B-1 through B-11 is included as Enclosure 1.

LOCATION: The meeting took place at the Franklin Room at the Crowne Plaza Hotel which is located at 14th & K Streets, N.W., Washington, DC 20005-3411.

Day 1/January 20, 1999

PARTICIPANTS: SAB Members (M), Consultants (C) and Staff: Dr. Mark Utell, Chair (M), Drs. Dr. John Doull (M), Dr. Grace K. LeMasters (M), Dr. Abby A. Li (M), Dr. Michele Medinsky (M), Dr. Frederica Perera (M), Dr. Roy E. Shore (M), Dr. Lauren Zeise (M), Dr. Richard Bull (C), Dr. Yvonne Dragan (C), Dr. Ernest McConnell (C), Dr. Kenny S. Crump (C), Dr. Lovell A. Jones (C), Dr. George Lambert (C), Dr. Roger O. McClellan (C), Dr. James Swenberg (C), Dr. M. Jane Teta (C), Ms. Roslyn Edson, Designated Federal Official (DFO), and Ms. Karen Martin, Life Scientist/EPA Intern (assigned to the SAB). The Committee Roster (incorporated as Attachment C) lists the Members and Consultants of the Cancer Guidelines Subcommittee who participated on the review. Their affiliations are included on the roster. A "Sign-In" sheet listing other attendees is incorporated as Attachment D-1 for January 20, 1999. Dr. William H. Farland, National Center for Environmental Assessment (NCEA) Director; Dr. Jeanette Wiltse, Office of Water; Dr. Vanessa Vu, NCEA; and Dr. James Cogliano, Group Director, Quantitative Risk Methods, NCEA were seated at the table along with the Committee Members and Consultants. The other EPA staff in attendance at the meeting included: Dr. Jack Fowle, Dr. Donald Barnes, Mark Mass, Stephanie Irene, Aparna Koppikar, Myra Karstadt, Kerry Dearfield, Karl Baetcke, Julie Du, Jennifer Jinot, Arnold Kuzmack, Amal Mahfouz, Steve Knott, Bill Wood, David Chen, Norb Hawkin, Robin Oshiro, and Ana Marie Gordon. There were approximately 70 members of the public.

SUMMARY: The meeting followed the Agenda with a few deviations in timing due to unanticipated extra time spent by the Members and Consultants who asked a variety of important, informational questions during the public comment sessions. The final agenda and the annotated agenda are incorporated as Attachment E-1 and E-2, respectively. The Members and Consultants were provided with blue folders which

contained material which is incorporated as Attachments F-1 through F-12. During the meeting, additional material (which is incorporated as Attachments F-13 through F-17) was distributed to the Members and Consultants only. The list describing the contents of Attachments F-1 through F-17 is included as Enclosure 1.

Before the meeting began, several handouts were made available on the table outside of the conference room. Those handouts are incorporated as Attachments G-1 through G-8. The list describing the contents of Attachments G-1 through G-8 is included in Enclosure 1.

Introductions

Dr. Mark Utell opened the meeting at 9:10 am and then turned the meeting over to Dr. Don Barnes, the Director of the Science Advisory Board. Dr. Barnes mentioned that a second SAB cancer guidelines meeting focused on children's health would take place in the near future and that the SAB was also planning to hold meetings on the application of chloroform and atrazine to the EPA Cancer Guidelines.

Public Disclosures

At 9:15 a.m., Roslyn Edson led the Subcommittee through the Public Disclosures process and focused its attention to the SAB Policy for Public Disclosures which was included in the blue folders and is incorporated in these minutes as Attachment F-5. Ms. Edson also introduced Ms. Wanda Fields, Management Assistant, and Ms. Karen Martin, EPA Intern assigned to the SAB.

Dr. Utell led the Public Disclosures session. He did express that the University of Rochester has a general interest in the EPA Cancer Guidelines and that he was involved in the past and currently in some research with the Health Effects Institute (HEI) and the EPA. He was a member of the Research Committee of HEI and is currently on the Board of the Annapolis Center.

Dr. Lovell Jones, the Director for Experimental Gynecology-Endocrinology in the Department of Gynecologic Oncology at the MD Anderson Cancer Center, informed the Subcommittee that his research was not directly related to the Cancer Guidelines but that he is a Member of the EPA Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC). Dr. Jones also mentioned that he would have to leave the meeting early and would return after he testified on the "Hill."

Dr. Kenny Crump, Vice President for KS Crump Group, Inc., has conducted research on some of the methodology that is included in the new Cancer Guidelines.

Dr. Yvonne Dragan, Assistant Professor at Ohio State University, has conducted carcinogenesis research and served on the International Life Sciences Institute (ILSI) Subcommittee that reviewed the cancer guidelines.

Dr. Richard Bull, a Senior Staff Scientist at Battelle Pacific Northwest National Laboratory, worked at the EPA 14 years ago. He has particular interest in the EPA Cancer Guidelines given his role as Chair of the EPA SAB Drinking Water Committee. Dr. Bull served on an ILSI chloroform steering group and conducted research related to the EPA Cancer Guidelines with the EPA and NASA.

Dr. Jane Teta, Director of Epidemiology, Health Information, Risk Assessment and TSCA for Union Carbide Corporation, has spent 10 to 12 years working with the American Industrial Health Council which submitted comments to the EPA on the Cancer Guidelines. She also served as Chair of the American Industrial Health Council (AIHC) panel and the Chemical Manufacturers Association (CMA) butadiene panel. Dr. Teta also wrote a paper which is not yet published on the application of the guidelines, using ethylene oxide. As an ILSI member, she gave public comments. Her salary is from Union Carbide which is a producer of chemicals and Dr. Teta has investments with Union Carbide.

Dr. George Lambert is an Associate Professor of Pediatrics and Director of Pediatric Pharmacology and Toxicology at the University of Medicine & Dentistry of New Jersey - Robert Wood Johnson Medical School; Attending Neonatologist at the Robert Wood Johnson University Hospital and St. Peter's Medical Center; and Director for the Center for Child and Reproductive Environmental Health in New Brunswick, New Jersey. He has conducted research on endocrine disruptors and their effect on human development.

Dr. Ernest (Gene) McConnell, EPA Science Advisory Panel Chair and President of Tox Path, Inc. conducted research with Dr. James Swenberg on combining tumor and tissue sites. Those data are referenced throughout the EPA's background material on the Cancer Guidelines. Dr. McConnell mentioned that the SAP will use the Cancer Guidelines in the future.

Dr. Roger McClellan, the President of the Chemical Industry Institute of Toxicology, gave an extensive public disclosure which included a description of CIIT as a not-for-profit research institution that is supported by chemical manufacturers. It was also mentioned that CIIT receives supplemental funding for research in which cancer is a disease endpoint. Dr. McClellan served on the ILSI chloroform steering group. He has made numerous public pronouncements, including congressional testimony. Dr. McClellan has advisory roles with several organizations including Resources for the Future and the Center for Risk Management. He has conducted research on the biological effects of low doses of radon and alternative toxicological methods.

Dr. Lauren Zeise is the Chief of the Reproductive and Cancer Hazard Assessment Section for the Office of Environmental Health Hazard Assessment at the California Environmental Protection Agency (CalEPA). Over the past 15 years, Dr. Zeise has worked extensively in the areas of risk assessment methodologies and cancer risk assessment. She has served as an expert witness in several court cases.

Dr. Michele Medinsky is a Toxicology Consultant. She conducts physiologically-based pharmacokinetic (PBPK) modelling research on hazardous air pollutants, many of which are known human carcinogens.

Ms. Edson, the DFO, was taking care of some other administrative issues, and therefore she was not available to take minutes when the following individuals gave their public disclosures:

Dr. James Swenberg, the Director for the Curriculum in Toxicology and a Professor of environmental Science and Engineering, Nutrition and Pathology at the University of North Carolina;

Dr. Abby Li, the Neurotoxicology Technical Leader at the Monsanto Company;

Dr. John Doull, Professor Emeritus, Department of Pharmacology, Toxicology and Therapeutics, University of Kansas Medical Center;

Dr. Roy Shore, Director, Division of Epidemiology and Biostatistics, New York University Medical School; and

Dr. Grace LeMasters, Director, Division of Epidemiology & Biostatistics,

Department of Environmental Health, University of Cincinnati.

After the public disclosures process, Ms. Edson reviewed the SAB Policy on Post-Report Activities which was included in the M/Cs packet and is incorporated as Attachment F-6.

Agency Briefing on the Revisions to the Cancer Guidelines

The Agency Briefing began at 10:00 a.m. Handouts 1 through 3 which are incorporated as Attachments H-1 through H-3 were distributed to the Members, Consultants and Members of the Public. Dr. William H. Farland, Director for the EPA National Center for Environmental Assessment, introduced the topic. Dr. Jeanette A. Wiltse, who works in the Health and Ecological Criteria Division in the Office of Water, continued with the briefing at 10:10 a.m. At 10:15 a.m., Dr. Vanessa Vu, Associate Director for Health Science for the National Center for Environmental Assessment, continued the briefing focusing on the Hazard Descriptors. At 10:25 a.m., Dr. James Cogliano, Group Director for the Quantitative Risk Methods of NCEA, discussed Dose Response Assessment. At 10:35 a.m., Dr. Janet Wiltse began talking about Mode of Action. A Member of the Subcommittee asked the Agency to compare the LD_{10} with the NOAEL to determine the impact on regulatory decisions. The Subcommittee also asked for clarification on the type of algorithm that the Agency was using. The response was that it was a polynomial model. The Agency's briefing ended at 11:05 a.m.

There was a discussion between the Subcommittee and the Agency regarding the material that was just presented. Some of the topics included: data on variability (citing an analysis by Hattison), the material on subpopulations, the EPA's use of modelling when cancer risk is 1-10%, the use of the ED_{10} vs. the LED_{10}, and Agency's policy on children and the developing child with regards to the Cancer Guidelines.

There was a lunch break from 12:05 a.m. until 1:10 p.m. Mr. Sam Rondberg gave some general comments about the content of the report, emphasizing that comments included in report must be made at the meeting or they cannot be considered in the report but that they can be added as an attachment to the report.

Public Comment Session

The public comment session began at 1:20 p.m. Dr. Utell gave each person a

maximum of 15 minutes to talk. The following individuals gave public comments.

1:20 p.m.	-	Dr. Matthew S. Bogdanffy, American Industrial Health Council (handout is incorporated as Attachment H-4),
1:43 p.m.	-	Dr. Clay Frederick, Chemical Manufacturers Association (handout is incorporated as Attachment H-5),
1:55 p.m.	-	Dr. Gail Charnley, Chlorine Chemistry Council (handout is incorporated as Attachment H-6),
2:00 p.m.	-	Dr. Daniel Byrd, III, Consultants in Toxicology, Risk Assessment and Product Safety, (handout is incorporated as Attachment H-7)(Dr. Byrd also submitted post-meeting comments that were received on February 2, 1999 and distributed to the Subcommittee on the same day. The comments are incorporated as Attachment I-1).
2:12 p.m.	-	Mr. Bill Kelley, Federal Focus, (mentioned that he planned to submit comments after the meeting to Ms. Edson),
2:20 p.m.	-	Ms. Lisa Lefferts, Mothers and Others for a Livable Planet, (handout incorporated as Attachment H-8),
2:30 p.m.	-	Mr. Jim Tozzi, Multinational Business Services, Inc.,
2:38 p.m.	-	Dr. David Wallinga, Natural Resources Defense Council, (handout incorporated as Attachment H-9), and
2:53 p.m.	-	Mr. James Wilson, Resources for the Future, was representing himself

The public comment session ended at 3:05 p.m. There was a break until 3:25 p.m.

When the meeting resumed, Dr. Frederica Perera gave her public disclosure. She mentioned published papers in peer reviewed journals and funding for research related to the Cancer Guidelines from NIEHS, EPA, DOD and private foundations.

At approximately 3:28 p.m., Dr. Vanessa Vu provided additional introductory comments on the International Agency for Research on Cancer (IARC) Criteria for Evaluation and the Biennial Report on Carcinogens. Copies of the three overheads that were used were distributed to the Subcommittee after the meeting, on February 2, 1999. That material is incorporated as Attachment I-2. During the meeting, Dr. Vu also referenced the letter from Kenneth Olden, National Institute of Environmental Health Sciences (NIEHS) director to Dr. Jim Tozzi, Director, Multinational Business Services, Inc.

regarding their September 21, 1998 letter to the Honorable Donna E. Shalala and Carol Browner on the listing of substances as "known human carcinogen."

Subcommittee Response to the Charge

Charge 1A: Do the proposed narrative summaries and the five hazard descriptors provide an appropriate and adequate basis for characterizing the technical evaluation of carcinogenic potential?

Charge 1B: Is the guidance supplied for each of the proposed hazard descriptors sufficiently clear and complete?

At 3:40 p.m., the Subcommittee began its discussion on Charge 1A and 1B. The Lead Discussant for Charge 1A was Dr. Perera and the Co-Discussants were Drs. LeMasters, Doull and Shore. Dr. McClellan was the Lead Discussant for Charge 1B and Drs. Shore, Perera, and LeMasters were the Co-Discussants. Some of the individual comments of the Subcommittee include the following:

1. Overall this section is a vast improvement over the 1996 Guidelines.
2. Consider removing "other key data" since this is a highly, speculative term.
3. Change "treatment related" to "exposure related."
4. The Subcommittee's guidelines should be consistent with the recommendations of the last SAB Committee that reviewed the Guidelines.
5. The EDSTAC report, when released, will establish a series of criteria that will trigger attention to look closely at chemicals that have not been tested.
6. There are not many chemicals for which there is adequate epidemiology to meet the "known" category criteria.
7. The classifications of "known" and "likely" should be separate.
8. Every group should be separated. One cannot use a basic descriptor.
9. The categories must be consistent and credible to the public.
10. The known category should be based on human data and the likely category should be based on animal data or whatever is available.
11. "Known" has a specific meaning and should not be combined with another category.

12. There needs to be some flexibility build into the 5 categories.

Charge 2A: Is the guidance provided in the revised Sections 2.3.5 - 2.5 clear and transparent?

At 4:50 p.m., the Subcommittee began its discussion on Charges 2A. The Lead Discussant for 2A was Dr. Swenberg and the Co-Discussants were Drs. Bull, Lambert, and Medinsky. Some of the individual comments included the following:

1. The strength and consistency issues on page 6 were an overall improvement.
2. The Mode of Action section was well-written and understandable. However, there are specific suggestions for clarity.
3. It may be useful to add in subpopulations such as children in the discussion on strength and sensitivity.
4. Section 2.5 was most helpful. Earlier sections did not provide the roadmaps. The examples were helpful.

The Chair concluded that all of the reviewers found that the Mode of Action section was strong.

Charge 2B: Please comment on the proposed key elements and their use in supporting a mode of action conclusion via the framework (Section 2.5).

The discussion on Charge 2B began at 5:00 p.m. The Lead Discussant for Charge 2B was Dr. Doull and the Co-Discussants were Drs. Swenberg, Lambert and Dragan. Some of the individual comments included the following:

1. Unlike the 1996 Cancer Guidelines, the revisions in the Mode of Action section bring everything together (eg. methods to count more precisely what determines the risk, i.e. rate limiting and rate determining, involves more peer review).
2. The default will probably rule most decisions.
3. Overall, this is well done. The Agency should continue to stress the pharmacokinetics and be careful about the definition of a precursor set.
4. It would be useful to indicate, in the mode of action section, that there will be additional recommendations for susceptible populations or groups and key

events.

5. Biological models should be considered. Hormonal endocrine disruptors do not follow the same course as chemical endocrine disruptors.

The Chair concluded that there was general support for the revisions to the Mode of Action section of the Guidelines.

Jack Fowle took over as Designated Federal Official at 5:20 p.m. The meeting adjourned at approximately 5:30 p.m.

Day 2/January 21, 1999

PARTICIPANTS: SAB Members (M), Consultants (C) and Staff: Dr. Mark Utell, Chair (M), Drs. Dr. John Doull (M), Dr. Grace LeMasters (M), Dr. Abby A. Li (M), Dr. Michele Medinsky (M), Dr. Frederica Perera (M), Dr. Roy E. Shore (M), Dr. Lauren Zeise (M), Dr. Richard Bull (C), Dr. Yvonne Dragan (C), Dr. Ernest McConnel (C), Dr. Kenny S. Crump (C), Dr. Lovell A. Jones (C), Dr. George Lambert (C), Dr. Roger O. McClellan (C), Dr. James Swenberg (C), Dr. M. Jane Teta (C), Ms. Roslyn Edson, Designated Federal Official, and Ms. Karen Martin, Life Scientist/EPA Intern (assigned to the SAB). The Committee Roster (incorporated as Attachment C) lists the Members and Consultants of the Cancer Guidelines Subcommittee who participated on the review. Their affiliations are included on the roster. A “Sign-In” sheet listing other attendees is incorporated as Attachment D-2 for January 21, 1999. The other EPA staff in attendance at the meeting included: Dr. Jack Fowle, Dr. Donald Barnes, Aparna Koppikar, Ann Marie Gordon, Julie Du, Robert McGaughy, Mark Mass, Jim Rowe, and Kerry Dearfield. There were approximately 50 members of the public.

Dr. Utell opened the meeting at 8:35 a.m. At 8:40 a.m., Dr. Utell gave a summary of the discussion that took place on the previous day. Regarding the Subcommittee's discussion on hazard descriptors, Dr. Utell outlined three options: 1) the "known" category should be broadened to "treat as known", 2) leave the "known" category as is but go back and broaden the definition because the current description is unclear and can lead one to different conclusions, and 3) use a category of regard as carcinogenic in human.

Dr. Utell also summarized the discussion on Mode of Action indicating that there was a lot of support for the framework on that section.

Subcommittee Discussion (continued)

Charge 2C: Are the case studies useful as illustrations of the guidance and framework?

The Subcommittee's discussion on Charge 2C began at 8:45 a.m. Dr. McConnell was the Lead Discussant and Drs. Jones, Swenberg, and Medinsky were the Co-Discussants. The following individual comments were made:

1. All three cases were quite useful and present 3 levels of data.
2. The first case was a strong one where the mode of action was operative. The first case lacks a discussion on how the exposure to the laboratory animals compares to that expected for humans.
3. The second case was not as strong as the first but there was still enough data to make a case that the mode of action was operative. There are some holes in the data and therefore, there are some value judgments.
4. In the third case, there was not enough data. This type of example is far more typical.
5. There should be cases that reflect children.
6. The EDSTAC report (which has not been released yet) has a few examples of non-classical cases.
7. The Agency is encouraged to develop more examples and to add a short section to the end of each case study to give a bottom line, in specific language, regarding the risk assessment that is being employed.
8. It was difficult to figure out when the timelines started.
9. The Mode of Action case studies need improvement, need to consider susceptible populations, and need to identify what is known about background exposure.
10. There is a big disconnect with these Mode of Action case studies. The Agency is using a non-linear mode of action which is not adddressed in these case studies.
11. The WHO meeting next month will bring forth ten such examples which will be presented to regulators.

Dr. Utell concluded this discussion by describing the Mode of Action case studies as a major step forward.

Charge 3A: Please comment on the soundness of the scientific rationale provided for

the standard approach and options for selecting departure points.

At 9:40 a.m., the Subcommittee began the discussion on Charge 3A. Dr. Zeise was the Lead Discussant and Drs. Li, Crump and McClellan were the Co-Discussants.

Some of the individual comments included the following:

1. Putting this information on the website is a really great development. However, the website location was not listed.
2. The EPA should provide additional guidance on problemmatic data sets.
3. More discussion on point of departure is needed on page 11 of the draft, revised guidance.
4, The labels used to distinguish between the two pathways of analysis should be clearer.
5. The Agency should try harder to develop approaches for continous data.
6. A section defining key terms should be added.

There was an extensive discussion about the choice of the central estimate vs. the confidence limit. A Subcommittee Member reiterated the Agency's rationale for selecting the confidence limit to clarify the justification. There was a concern about the use of the Faustman, et. al, 1994 paper on pages 6 and 7 of Section 3. It was also mentioned that the reference to Porter's work as an option and the rationale for choosing the LED_{10} was unclear and the citation was wrong. The accompanying paper by Allen was identified as the correct citation for the data.

Charge 3B: Please comment on the adequacy and clarity of the guidance on this subject.

At 10:15 a.m., the Subcommittee discussion on Charge 3B began. The Lead Discussant was Dr. Crump and the Co-Discussants were Drs. Li, Zeise, and McConnell. There was some discussion on the previous SAB report on the proposed EPA Cancer Guidelines. The Subcommittee discussed pages 8 and 24 of that report. The second paragraph on page 24 was read to the Subcommittee by one of the Members. There was a similar difference of opinion regarding the point estimate vs. the statistical bounds amongst the Subcommittee as there was amongst the EHC that reviewed the proposed Guidelines in 1997. During the discussion on Charge 3B, a

member of the Subcommittee asked if the discussion on TEF in the old Section 3.1 would be retained and the Agency responded, "yes."

There was a break from 10:50 a.m. until 11:15 a.m.

Charge 4A: Please comment on the adequacy and clarity of the guidance regarding how to perform a MOE analysis.

The Subcommittee discussion on Charge 4A began at 11:15 a.m. The Lead Discussant was Dr. Crump and the Co-Discussants were Drs. Jones, Teta and Zeise. The individual comments included the following:

1. The Agency did a good job on this section.
2. Has the Agency looked at different ways to look at the safety factors, e.g. adding the square roots?
3. An additional safety factor for severity was recommended.
4. There was a concern regarding the separation of policy from science.
5. There was a concern regarding the safety factor of 3.
6. There was a concern regarding the use of biomarkers without an endpoint specified.
7. There should be more clarity on the safety factors and data on human variability should be included.
8. There was a concern about the use of safety factors in relation to key events and the biological basis for the safety factors was unclear.

Dr. Shore presented overheads describing heterogenicity and sensitivity with regards to exposure to ionizing radiation. He presented data on differences due to gender, ethnicity, and age. The data was descibed as an example where the 10 fold guidelines for heterogencity are adequate. Copies of some of the material was received, upon request, on February 16, 1999, and placed in the FACA file. This material is incorporated into the minutes as Attachment J-1.

There was a lunch break from 12:25 p.m. until 1:33 p.m.

The meeting resumed at 1:33 p.m. Dr. Cogliano presented an overhead comparing the 96 Proposed Cancer Guidelines with the Current Draft. A copy of the overhead was

requested after the meeting and is incorporated as Attachment J-2.

Abby Li presented data on the application of the LED_{10} and the NOAEL. A copy of the overhead was requested after the meeting. It was received on February 18 and is incorporated as Attachment J-3.

Dr. Perera left the meeting at 2:00 p.m.

Charge 4B: Are the proposed approach and the factors for consideration in determining the appropriate magnitude of the MOE appropriate? Specifically address the use of factors to account for:

(1) the nature of the response (i.e., tumors or key events selected as the point of departure for extrapolation)
(2) steepness of the dose response curve
(3) human intraspecies variability, including susceptible populations
(4) interspecies variability.

The Subcommittee discussion on Charge 4B began at 2:00 p.m. The Lead Discussant was Dr. Crump and the Co-Discussants were Drs. Shore, Teta, and Dragan. In addition, the other Members and Consultants of the Subcommittee were asked comment on this question. Some of the individual comments included the following:

1. There was a concern about the selection of the safety factor in the thyroid example.
2. It was difficult to sort out some of the logic in the thyroid example, including the types of measurements used to establish key events.

At 2:15 p.m., Dr. Utell summarized the Subcommittee's Charge responses. He began with the discussion on the Hazard Descriptors. Dr. Utell reiterated the three possible approaches to addressing this issue: 1) use the structure that the Agency presented but give more detail; 2) combine known with "to treat as known"; and 3) use a category of regard or treat as a human carcinogen. Dr. Utell also stated that there was some agreement that “known” should be defined within fairly narrow bounds. The Mode of Action section was described by the Chair as having general support from the Subcommittee and as needing additional discussion on subpopulations. The

discussion regarding the Dose-Response section was described as similar to that of the EHC during its 1997 review of the proposed EPA Cancer Guidelines and that the advice in the paragraph read from the previous SAB report by Dr. Zeise would probably be similar to this Subcommittee's advice to the Agency. The Subcommittee also recommended that, in future SAB reviews, the Agency reprint the entire text including the revisions because it was difficult to put all the pieces together and refer back to the unrevised text in the 1996 proposed guidelines. In terms of the Margin of Exposure, Dr. Utell stated that the safety factors in the case studies need clarification. Dr. Utell concluded that the Subcommittee recommends additional revisions to the hazard descriptors and the margin of exposure sections. Finally, it was emphasized by the Chair that there was some urgency in finalizing and publishing the Guidelines. The initial issuance of the Revised Guidelines dates to 1996. Note that the revised guidelines were first reviewed by the Environmental Health Committee in February 1997.

I certify that these minutes are accurate to the best of my knowledge.

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Dr. Mark Utell, Chair Cancer Guidelines Subcommittee of the Executive Committee	Ms. Roslyn Edson Designated Federal Official

MINUTES OF THE CANCER GUIDELINES SUBCOMMITTEE OF THE SAB EXECUTIVE COMMITTEE JANUARY 20-21, 1999

ENCLOSURE 1

Attachment A — Federal Register announcement

Attachment B — Background Material

- B-1 Memorandum dated December 22, 1998 from Roslyn Edson, Designated Federal Official (EPA, SAB) to Cancer Guidelines Subcommittee Members and Consultants (with B-2 through B-6 attached)
- B-2 Draft Public Roster
- B-3 Cancer Guidelines Revisions
  - i) Section 2.3.5, *Key Events Relevant to Mode of Carcinogenic Action*,
  - ii) Section 2.5, *Evaluating a Postulated Mode of Action,*
  - iii) Section 2.6.2, *Descriptors for Summarizing Weight of Evidence,*
  - iv) Section 3, *Dose Response Assessment,*
  - v) Appendix D, *Framework for Mode of Action Analysis, Example 1, Chemical T (Thyroid Disruption),*
  - vi) Appendix D, *Framework for Mode of Action Analysis, Example 2, Chemical Z (Bladder Tumor),*
  - vii) Appendix D, *Framework for Mode of Action Analysis, Example 3, Chemical D,*
  - viii) Appendix E, *Nonlinear Dose-Response: Margin of Exposure Analysis, Example 1,*
  - ix) Appendix E, *Nonlinear Dose-Response: Margin of Exposure Analysis, Example 2*,
  - x) Appendix E, *Nonlinear Dose-Response: Margin of Exposure Analysis, Example 3: Chemical T (Thyroid Disruption)*,
- B-4 *Federal Register, Tuesday, April 23, 1996: Part II, Environmental Protection Agency, Proposed Guidelines for Carcinogen Risk Assessment; Notice*

B-5 An SAB Report: Guidelines for Cancer Risk Assessment, Reviev the Office of Research and Development's Draft Guidelines for Cancer Risk Assessment by the Environmental Health Committe September 1997 (EPA-SAB-EHC-97-010), and

B-6 Letter dated March 13, 1998 from Henry Longest, II, Acting Assi Administrator, ORD, to Dr. Joan Daisey, Chair, SAB, Subject: Response to SAB Review of the Proposed Revised Guidelines f Carcinogenicity Risk Assessment (EPA-SAB-EHC-97-010)

B-7 December 31, 1998 memo from Roslyn Edson to Cancer Guideli Subcommittee, subject: draft Charge, Assignments, Schedule fo Report Preparation, and letter from the Multinational Business Services, Inc.

B-8 January 4, 1999 memo from Roslyn Edson to Cancer Guidelines Subcommittee, subject: Final Charge

B-9 January 7, 1999 letter from Jim Wilson to the SAB Cancer Guidelines Subcommittee re: comments on revised Guidelines, received on January 13, 1999 and sent to the Subcommittee on January 13, 1999

B-10 January 14, 1999 memo from Roslyn Edson to Cancer Guideline Subcommittee, subject: draft agenda and list of the sections of th Cancer Guidelines that have been revised

B-11 January 15, 1999 memo from Roslyn Edson to the Cancer Guidelines Subcommittee with attached comments from the Natu Resources Defense Council

Attachment C Subcommittee Public Roster

Attachment D — Sign-In Sheets

- D-1 January 20, 1999
- D-2 January 21, 1999

Attachment E — Agendas

- E-1 Original agenda
- E-2 Annotated agenda

Attachment F — Handouts to Members and Consultants in blue folders

- F-1 Final Agenda
- F-2 Charge
- F-3 Full Roster
- F-4 Final Charge and Assignments
- F-5 Policy for Public Disclosures at SAB Meetings with Appendix A, Mock Disclosure
- F-6 Policy on Post-Report Activities, January 15, 1997
- F-7 Schedule for Report Preparation
- F-8 Comments on 12/21/98 Draft Revisions of EPA Proposed Cancer Risk Assessment Guidelines (Margin of Exposure M.J. Teta, Dr.P.H., January 20-21, 1999
- F-8 Section 3: Dose Response Analysis, Draft Comments fror Abby Li
- F-9 Breast Cancer Action letter dated January 19, 1999 to Ca Browner re: Cancer Risk Assessment Guidelines
- F-10 American Forest & Paper Association letter dated Januar 19, 1999 to Dr. Mark Utell re: Cancer Guidelines - reques for extension of time to comment
- F-11 Resources for the Future letter to SAB Cancer Guidelines Subcommittee dated January 7, 1999, subject: comments on Revised Guidelines

F-12 Letter from the Natural Resources Defense Council to Donald G. Barnes, SAB Staff Director, dated January 15, 1998, re: comments on revisions to the EPA Proposed Guidelines for Carcinogen Risk Assessment

Additional Material Added to Folders During the Meeting

F-13 Written Comments Completed by Grace Lemasters for January 21-22, 1998

F-14 Frederica Perera's Comments in a letter to Dr. Utell, date January 19, 1999

F-15 George Lambert's Comments for January 20 and 21, 199 SAB meeting

F-16 Comments for Advisory for Cancer Risk Assessment Guidelines from RJ Bull, dated 1/17/98

F-17 Comments to the U.S. EPA Science Advisory Board (Cancer Guidelines Subcommittee), Regarding "Proposed for Carcinogen Risk Assessment," Roy E. Shore, January 19, 1999

Attachment GMaterial Made Available to the Public just prior to the Meeting (placed on the table lo directly outside the meeting room)

G-1 Agenda

G-2 Subcommittee Public Roster

G-3 Charge

G-4 Charge Questions and Assignments

G-5 Resources for the Future letter to SAB Cancer Guidelines Subcommittee dated January 7, 1999, subject: comments on Revised Guidelines (also F-11)

G-6 Breast Cancer Action letter dated January 19, 1999 to Carol Browner re: Cancer Risk Assessment Guidelines (also F-9)

G-7 Natural Resources Defense Council letter dated December 21, 1 to Carol Browner, EPA Administrator: re: concerns re: SAB Canc Guidelines meeting scheduled for January 20-21, 1999

G-8 Multinational Business Services, Inc. Letter dated December 29, 1998 to Dr. Joan Daisey, SAB Executive Committee Chair and D Mark Utell, EHC Chair

re: “Known Human Carcinogen”

Material Distributed During the Meeting

Attachment H

H-1	Handout 1/Day 1, Carcinogen Guidelines Revisions Advisory Meeting Introduction by USEPA Risk Assessment Forum Technical Panel
H-2	Handout 2/Day 1, The White House, Office of the Press Secretary, Exe Order, Protection of Children From Environmental Health Risks and Sa Risks, April 21, 1997
H-3	Handout 3/Day 1, Questions and Answers Regarding Application of Ex Order 13045 and EPA’s Policy on Evaluating Health Risks to Children
H-4	Handout 4/Day 1, Comments on: Proposed Guidelines for Carcinogen Assessment by Matthew S. Bogdanffy, Ph.D., D.A.B.T., Chair, Dosimet and Risk Assessment Subcommittee, American Industrial Health Coun
H-5	Handout 5/Day 1, Remarks of Dr. Clay Frederick on behalf of CMA - Ja 20, 1999 SAB Meeting
H-6	Handout 6/Day 1, EPA Science Advisory Board, Advisory on Proposed Revised Guidelines for Carcinogen Risk Assessment, 20 January 1999 Transcript of Comments Provided by Gail Charnley, Ph.D.
H-7	Handout 7/Day 1, An Excerpt from Comments by Consultants in Toxico Risk Assessment and Product Safety to the U.S. Environmental Protec Agency about a review draft of *Carcinogenic Effects of Benzene: An Update* (EPA/600/P-97/001A; June, 1997)
H-8	Handout 8/Day 1, Statement on Revisions to the EPA Proposed Guidel for Carcinogen Risk Assessment, Lisa Y. Lefferts, Science Advisor to Mothers & Others for a Livable Planet, January 20, 1999 Science Advis Board Meeting
H-9	Handout 9/Day 1, letter from the Natural Resource Defense Council to Donald G. Barnes, SAB Staff Director re: comments on revisions to the

Proposed Guidelines for Carcinogen Risk Assessment (amended), date
January 20, 1998

H-10 Handout 10/Day 1, letter from Dr. Kenneth Olden, NIEHS Director, to Ji
Tozzi, Ph.D., Director, Multinational Business Services, Inc. Re: their
September 21, 1998 letter to the Honorable Donna E. Shalala and Carc
Browner re: listing substances as “known human carcinogen”

Material Distributed After the Meeting and Distributed to the Subcommittee and Members of the Public Who Requested the Material

Attachment I

I-1 February 2, 1999 fax from Roslyn Edson to the Subcommittee with postmeeting comments from Dr. Daniel Byrd, Consultants in Toxicology Assessment and Product Safety, dated February 1, 1999

I-2 February 2, 1999 fax from Roslyn Edson to the Subcommittee with cop 3 additional overhead transparencies presented by Dr. Vanessa Vu, on (Topics were: Biennial Report on Carcinogens: Criteria for Listing, Rep Carcinogens, and IARC Criteria for Evaluation)

Material Requested by Designated Federal Official and Placed in the FACA File After the Meeting

J-1	Some of the overheads presented by Dr. Roy Shore on January 21, 19
J-2	Copy of overhead presented by Dr. Jim Cogliano on January 21, 1999
J-3	Copy of overhead presented by Dr. Abby Li on January 21, 1999